ABSTRACT

Disclosed are methods for determining the stage of neurofibrillary degeneration associated with a tauopathy in a subject believed to suffer from the disease, which methods comprise the steps of: (i) introducing into the subject a ligand capable of labeling aggregated paired helical filament (PHF) tau protein, (ii) determining the presence and/or amount of ligand bound to extracellular aggregated PHF tau in the medial temporal lobe of the brain of the subject, (iii) correlating the result of the determination made in (ii) with the extent of neurofibrillary degeneration in the subject. The methods can be used for pre-mortem diagnosis and staging of tauopathies such as Alzheimer's Disease. Preferred ligands include sulphonated-benzothiazole-like compounds and diaminophenothiazines. Novel ligands (e.g. sulphonated-benzothiazole-like compounds) are also provided. The method may also include the use of "blocking ligands" to block competing binding sites. In other aspects the invention provides in vitro methods for identifying ligands capable of labeling aggregated PHF tau protein, the methods comprising the steps of: (i) providing a first agent suspected of being capable of labeling aggregated PHF tau protein, (ii) contacting (a) a tau protein or a derivative thereof containing the tau core fragment bound to a solid phase so as to expose a high affinity tau capture site, with (b) a liquid phase tau protein or derivative thereof capable of binding to the solid phase tau protein or derivative, and (c) said selected first agent and (d) a second agent known to be tau-tau binding inhibitor, (iii) selecting first agent which fully or partially relieves the inhibition of binding of the liquid phase tau protein or derivative of (b) to the solid phase tau protein or derivative of (a) by the inhibitor (d).

Ligands may also be tested to confirm that they are not themselves inhibitors.